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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/890,088	07/26/2001	Alessandro Lambiase	36226/125733	6075

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EXAMINER
DI NOLA BARON, LILIANA

ART UNIT	PAPER NUMBER
1615	

DATE MAILED: 05/20/2003

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/890,088	LAMBIASE, ALESSANDRO	
	Examiner	Art Unit	
	Liliana Di Nola-Baron	1615	

-- The MAILING DATE of this communication appears n the cover sheet with the corresp ndence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 April 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *13-24* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *13-24* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Receipt of Applicant's response, filed on April 1, 2003, is acknowledged.

Claim Rejections - 35 USC § 102

1. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

2. Claims 13-20 are rejected under 35 U.S.C. 102(a) as being anticipated by WO98/10785. The patent provides an ophthalmic composition for subconjunctival and ocular injection to treat optic nerve disorders, said composition comprising NGF in an amount of 10^{-3} to 2x 10^{5} μg/l (See pp 3-4), corresponding to a maximum amount of 200 μg/ml, which is in the range claimed by Applicant in claim 1 and meets the limitations of claims 19 and 24.

The method disclosed by the patent meets the limitations of claims 13-20 of the instant application, as it contemplates methods comprising administering a composition comprising nerve growth factor (NGF) to a subject in need thereof for the treatment of a pathology affecting the internal tissue of an eye. Thus, the patent anticipates the claimed invention.

Claim Rejections - 35 USC § 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person

having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

4. Claims 13-24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Finkenaur et al. (EPA 0312208A1).

Finkenaur et al. discloses the use of a composition comprising a polypeptide growth factor, in particular NGF, in a concentration of 1-500 μg/ml for the treatment of wounds (See p. 4, lines 7-13), teaches that the gels of the invention can be in the form of eye drop formulations or solutions, includes surgically induced ophthalmic wounds, which result, among others, from corneal ulcers or corneal transplants, among the wounds healed by the composition of the invention and defines ophthalmic wound healing as including anterior chamber wound healing as well as subconjunctival wound healing (See p. 6, lines 3-11). Additionally, Finkenaur et al. teaches that the gel of the invention can be applied to internal wounds and gel-forming polymer can be degradable (See p. 6, lines 12-13).

Thus, Finkenaur et al. contemplates the treatment of ophthalmic wounds, which can damage intraocular tissues, such as the anterior chamber of the eye, or the subconjunctival tissue (See p. 6, lines 3-11). Finkenaur et al. does not specifically mention that the compositions of the invention are administered into the ocular surface, however, the eye drop formulations and ophthalmic irrigating solutions contemplated by Finkenaur et al. are suited for application into the ocular surface of the eye, as claimed by Applicant.

Therefore it would have been obvious to one having ordinary skill in the art at the time the invention was made to apply the teachings of Finkenaur et al. to device methods for the treatment of pathologies affecting the internal tissue of an eye, comprising administering NGF in the amount disclosed in the publication. The expected result would have been successful methods of treatment of the pathology in the eye. Because of the teachings of Finkenaur et al., that NGF is effective in treating ophthalmic wounds, including internal wounds, one of ordinary skill in the art would have a reasonable expectation that the methods claimed in the instant application would be successful. Therefore the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Response to Arguments

5. Applicant's arguments filed on April 1, 2003, have been fully considered but they have been found only partially persuasive.

6. Applicant argues that Finkenaur et al. only incidentally mentions NGF and teaches various growth factors having different individual molecules with different amino acid sequence, structure and molecular weight, different receptor sites and different biological activity. In response to said argument, it is noted that Finkenaur et al. specifically include NGF among the growth factors used in the invention. Furthermore, Applicant's invention is directed to a composition comprising NGF and does not read on specific amino acid sequence, structure, molecular weight, receptor sites and biological activity.

7. Applicant's argument, that Finkenaur et al. does not teach that the formulations are administered into the ocular surface of the eye have been found persuasive with respect to the 35

U.S.C. 102 (b) rejection of claims 13-24 of the previous Office action. Accordingly, said rejection is withdrawn. However, Finkenaur et al. is considered relevant under 35 U.S.C. 103(a), for the teachings that the compositions of the invention may be in the form of eye drop formulations and ophthalmic irrigating solutions, which are suited for application into the ocular surface of the eye, as claimed by Applicant.

8. Applicant's arguments regarding the 35 U.S.C. 102(e) rejection of claims 13-20 over Louis of the previous Office action have been found persuasive, since the prior art teaches GDNF, which is different from the nerve growth factor claimed by Applicant. Accordingly, said rejection is withdrawn.

9. In response to Applicant's argument, that Okamoto discloses a much broader concentration range than Applicant's, it is noted that the reference discloses composition comprising NGF in an amount of 10^{-3} to 2x 10^{5} μg/l (See pp 3-4), corresponding to a maximum amount of 200 μg/ml, which is in the range claimed by Applicant in claim 1 and corresponds to the amount claimed by Applicant in claims 19 and 24. Thus the reference anticipates the claimed invention.

10. Applicant's arguments regarding the 35 U.S.C. 103(a) rejection of claims 13-24 over Finkenaur et al. have been addressed above. With regard to Applicant's argument, that Finkenaur et al. does not teach or suggest that NGF is able to pass through the ocular tissues, so that the composition is applied only to the ocular surface, it is noted that the reference teaches that the compositions of the invention may be in the form of eye drop formulations and ophthalmic irrigating solutions, which are suited for application into the ocular surface of the eye, as claimed by Applicant. Furthermore, the features upon which Applicant relies (i.e., passing through the

ocular tissues) are not recited in the rejected claims. Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

11. Applicant's arguments regarding the 35U.S.C.103(a) rejection of claims 13-24 over Hammang et al. of the previous Office action have been found persuasive, since the prior art teaches a dosage range, which is lower than the range claimed by Applicant. Accordingly, said rejection is withdrawn.

12. Applicant's arguments regarding the 35 U.S.C. 103(a) rejection of claims 13-24 of the previous Office action over Reich in view of Finkenaur et al. have been found persuasive, since Reich does not teach that the compositions of the invention may be administered into the ocular surface as claimed by Applicant. Accordingly, said rejection is withdrawn.

Conclusion

13. Claims 13-24 stand rejected.

14. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37

CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Liliana Di Nola-Baron whose telephone number is 703-308-8318. The examiner can normally be reached on Monday through Thursday, 5:30AM-4:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman K Page can be reached on 703-308-2927. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3592 for regular communications and 703-305-3592 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 308-1234/ 1235.

May 9, 2003

THURMAN K PAGE
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600